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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/624,131	07/21/2000	Ravi Kapur	97,223-1	4910

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EXAMINER

COOK, LISA V

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 03/25/2002

6

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/624,131

Applicant(s)

KAPUR ET AL.

Examiner

Lisa V. Cook

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-13 is/are rejected.
- 7) ☒ Claim(s) 13 and 14 is/are objected to.
- 8) ☒ Claim(s) 1-14 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

1. Applicants' election with traverse of Group IV (claims 11-14) in Paper #5, filed 2/4/02 is acknowledged. Applicant does not traverse the Restriction Requirement on the grounds of lack of patentable distinctness. The traversal on the ground(s) "that the Examiner is not seriously burdened by the scope of the search required to examine all the pending claims (Groups I-IV)", thus the burden to require restriction does not exist and the inventions are sufficiently related to preclude restriction notwithstanding the existence of patentable distinctness, is not found convincing.

This is not found persuasive because MPEP § 808.02 recites:

Where related inventions as claimed are shown to be distinct under the criteria of MPEP § 806.05(c)- § 806.05(i), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof, (B) A separate status in the art when they are classified together, or (C) A different field of search.

In the instant case, (A) -The Restriction Requirement under 35 U.S.C. § 121 in Paper #3, mailed 10/2/01 established distinctness of the inventions and separate classification thereof:

(B) The inventions of Groups I-IV would require a separate status in the art when they are classified together. The combined inventions when classified together are directed to methods detecting toxin pathway and organ localization, which would be classified in class 436, subclass 514, for example.

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(C) With respect to a different field of search – Because these inventions are distinct and have acquired separate status in the art as shown by their different classification, recognized divergent subject matter and because the search required for each invention is not substantially coextensive with the search required for the remaining invention, restriction for examination purposes as indicated is proper. Please note that the classifications in the restriction are illustrative only and do **not** represent all the classes and subclasses, which must be searched for each invention; nor is the search limited to issued US patents, but rather includes published foreign patents and applications as well as literature search.

2. For these reasons the inventions of Group I-IV were not joined.

The Restriction Requirement is still deemed proper and is therefore made **FINAL**.

3. Currently, claims 1-14 are subject to Restriction and Election Requirement. Claims 1-10 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as claims drawn to a non-elected invention. Claims 11-14 are pending and under examination.

Priority

4. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). The cross-reference section should be updated to include patent # 6,103,479. (i.e. 08/865,341, filed on May 29, 1997, now Patent #6,103,479. Please add to the specification.

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

Drawings

6. The drawings in this application are objected to by the Draftsperson as informal. Any drawing corrections requested, but not made in the prior applications should be repeated in this application if such changes are still desired. If the drawings were changed and approved during the prosecution of the prior applications, a petition may be filed under 37 CFR 1.182 requesting the transfer of such drawings provided the parent application has been abandoned. However, a copy of the drawings as originally filed must be included in the 37 CFR 1.60 application papers to indicate the original content.

Specification

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

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I. The disclosure is objected to because of the following informalities:

On page 66, lines 26-27, for example large spaces occur between the words. It is not clear if these are merely spacing errors or are words actually missing. Please correct.

On page 70, lines 28-31, for example single spaced lines are employed.

The spacing of the lines of the specification is such as to make reading and entry of amendments difficult. New application papers with lines double spaced on good quality paper are required. See page 69, lines 12-19, page 78 lines 1-1, and page 80 lines 13-25 for examples.

II. The use of the trademarks has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Double Patenting

8. Double patenting obviousness-type rejection:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 11-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Application No. 09/513,783. Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions are drawn to cell analysis procedures employing the same method wherein multiple luminescent-labeled reporter molecules are used to label the protein of interest, the cell, and location. Therein the instant invention is encompassed within Application #09/513,783 wherein a cell is analyzed via the same method.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable Taylor et al. (Optical Diagnostics of Living Cells and Biofluids, Vol. 2678, 1996, pages 15-27) or Taylor et al. (American Scientist, 80:322-335, 1992) in view of Hendzel et al. (Chromosoma, 1997, 106:348-360).

Taylor et al. (Optical Diagnostics of Living Cells and Biofluids) teach new technologies used in conjunction with light microscopy to measure events in living cells via an automated method. The new automated methodology involves cell imaging and scanning techniques that are extrapolated to identify signal as digital data subsets for further analysis (multidimensional image data). See page 16, 3rd and 4th paragraphs.

Taylor et al. (American Scientist) teach new technologies used in conjunction with light microscopy to measure events in living cells. One major advance of the new methodology is found in the use of computers for digital processing and analysis of images. Another improvement is seen in the development and use of fluorescent dyes, which can be attached to specific molecular structures thereby revealing the location of those structures in the cells. Dye molecules can also be designed so that their fluorescence is controlled by specific physiological changes; thus they indicate what is happening in the cells, as well as when and where (page 322,

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column 3, 1st paragraph). Taylor et. al. teach modified multi-mode light-microscope workstations that incorporate multiple electronic detectors and provide computer control of all major microscope functions. Images are converted to a digital form that can be read and manipulated by the computer (pages 324 & 325). Taylor et. al. teach indicators that reveal where a marker has gone in the cell and what conditions exist in that area, as well as the use of more than one tagging molecule with one or more suitably chosen fluorescent labels to learn whether or not the molecules are close to each other in the cell. When one label is stimulated to fluorescence, it can transfer part of its energy to the second label molecule, leading to fluorescence at another wavelength (page 328, figure 8). Thus meeting the limitation of dual luminescent reporter wherein one is a detector and the other is a classifier. Taylor et. al. also teach the measuring of changes in excitation or emission spectrum of an indicator using a mode of microscopy known as ratio imaging which relies on digital post-processing. The method is exemplified by the measurement of calcium concentration (applicant's toxin).

Two images are recorded, one in the calcium-sensitive part of the spectrum and the other at a calcium-independent wavelength, then all the pixel intensities of the Ca²⁺ sensitive images are divided by those of the Ca²⁺ independent image. The resulting ratio image is normalized for variations in the optical path length, in the volume accessible to the calcium probe and in the concentration of the probe, and provides a map of the intercellular concentration of free calcium ions.

Taylor et al. and Taylor et al. differ from the instant invention in failing to teach multiple cell analysis comprising two or three cell types with respect to toxin (test compound exposure).

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However, Hendzel et al. teach the relationship between H3 phosphorylation and mitotic chromosome condensation in mammalian cells. The precise spatial and temporal correlation of chromatin is evaluated. (abstract and page 349 –1st column) Nuclear mask or nuclear staining images are compared and correlated to the various phases of mitosis (mitotic index). See page 353 Progression of H3. Dual staining procedures to evaluate location and mitotic state are described (anti-phosphorylated H3 “red” and ACA autoimmune “green” sera). See page 354, 2nd column. The method is evaluated with respect to the L929(murine), C6 glioma (rat), HeLa(human), SAOS-2(human), and Indian muntjac cell lines. See page 352, 2nd column, 1st paragraph, last sentence and page 354, 2nd column 1st paragraph, last sentence. Hendzel et al. further teaches that several cells could be analyzed via digital imaging (Vaytek MicroTome Software) allowing for the removal of out of focus information (adjacent sections), point spread functions, rescaling, and color co-localization images. See pages 350-351.

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure multiple cell types as taught by Hendzel et al. in the methods Taylor et al. and Taylor et al., to assay one compound in several cell lines further analyzing them to generate a complete schematic of toxin detection and organ localization effects as a whole, because Hendzel et al. taught that different cell type evaluation resulted in various specific detection parameters which could be analyzed to give an accurate account of co-localization through digital con-focal microscopy (Hela, SKN, and Indian muntjac cells). See page 354, 2nd column, 2nd paragraph, last sentence and page 352, 2nd column, lines 5-7.

12. For reasons aforementioned, no claims are allowed.

Remarks

13. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Price et al. (USP# 5,790,710) disclose an autofocusing system for obtaining measurements of fluorescent stained cellular components by scanning multiple microscope fields.

B. Harpold et al. (USP# 5,436,128) teach methods for detecting and evaluating intracellular transduction on extracellular signals.

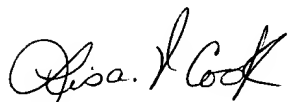
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14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

 3/24/02
Lisa V. Cook
CM1-7B17
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CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800/691